

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow. As the following paragraphs explain, Applicants believe that each of the rejections and objections is overcome, placing the case in condition for allowance. Accordingly, an early indication of allowability is respectfully requested.

Applicants have added Claim 22. The original specification supports claim 22, for example, in Table 1 on page 18, in Table 5 bridging pages 69 and 70, and in the paragraph bridging pages 75 and 76. Following entry of these revisions, claims 14-22 will be pending. Claims 19-21 are withdrawn. Applicants reserve the right to file a divisional application as a vehicle for the subject matter of any withdrawn claims.

The specification has been amended to insert SEQ ID NOs and to delete embedded hyperlinks. No new matter is introduced by this revision.

Response to Restriction Requirement/Election of Species and Interview Summary

Applicants confirm election of Group 1, claims 14-18, as well as species election characterized by ERGIC-53. Applicants' representative, Yang Tang, made the election by telephone on February 21 and March 1, 2006.

Based on the teleconferences, Applicants subsequently filed a reply on March 2, 2006 to include the substance of the interview. A copy of the previously filed reply is attached for the Examiner's convenience. Applicants respectfully request the Examiner acknowledge receipt of the reply in the next action.

Priority Claim under 35 U.S.C. §119(a)-(d)

To obtain the benefit of foreign priority under 35 U.S.C. § 119(a)-(d), Applicants submit the accompanying, certified English translation of Japanese Patent Application No. 2002-238559.

Objection to Drawings

In Section 11 of the action, the Examiner has objected to Figure 3 and requested the Applicants to “amend the specification to delete any Figures which consist only of nucleic acid or protein sequences...” (emphasis added). Figure 3 is a diagram depicting VIP36 random mutations in the vector. Therefore, Figure 3 should not be deleted as it contains additional information other than nucleic acid or protein sequences. Accordingly, Applicants respectfully request the Examiner withdraw her objection to Drawings.

Sequence Rule Compliance

In compliance with 37 C.F.R. §1.821 through §1.825, Applicants submit herewith an updated Sequence Listing in paper and in computer readable form, along with a statement to support filing the Sequence Listing.

Rejections Under 35 U.S.C. §112 first paragraph

In Sections 14 and 15 of the Office Action, the Examiner has rejected claims 14-18 for failing to comply with the written description requirement. Applicants respectfully disagree.

As the specification describes in detail, a eukaryotic cell of the present invention comprises a heterologous DNA coding for a modified cargo receptor. In a plurality of such cells, a different cell may contain a heterologous DNA coding for a different cargo receptor, such that the plurality *in toto* expresses a variety of glycoproteins with different carbohydrate moieties. With these ideas in mind, Applicants have revised Claim 17 to set out the claimed subject matter more clearly.

On page 10 of the action, the Examiner contends that the “instant specification recites examples of cells comprising only one type of heterologous cargo receptor” (second full paragraph, third sentence). On the contrary, the present specification in fact illustrates a variety of heterologous cargo receptors. Thus, Example 1 describes a variety of heterologous DNAs, prepared by random mutagenesis, that code for modified cargo receptors. The DNA library thereby obtained contains 6 to 8×10^5 randomly mutated DNA. Subsequently, the

mutated DNA is transfected into cells and the expression of the mutated cargo receptors is assayed in Example 2. Accordingly, the specification fully supports the present recitation of a plurality of eukaryotic cells, comprising heterologous DNA coding for a variety of modified cargo receptors, per Claim 17.

The Examiner also alleges that the instant application does not “identify a wild-type glycoprotein from which the carbohydrate moiety could be modified” (page 10 of the action, the third full paragraph). The present invention, however, is not limited to a particular glycoprotein from which the carbohydrate moiety could be modified.

As the specification describes in the paragraphs from page 21, line 13 to page 22, line 14, the glycoprotein can be either an endogenous glycoprotein or a heterologous glycoprotein, expressed and glycosylated in a cell. In other words, the present invention embodies an inventive concept, which entails modifying the carbohydrate moiety of a glycoprotein during the process of sorting the glycoprotein via secretory pathways. A cargo receptor, illustrated by ERGIC-53 and VIP-36 in the present application, functions in sorting and transporting glycoproteins in secretory pathways. When the cargo receptor is altered, the resultant alteration of the secretory pathway effects addition of a different carbohydrate to a glycoprotein.

Thus, the present invention is limited neither to modifying a particular carbohydrate moiety of a certain glycoprotein nor to the use a given carbohydrate moiety. Rather, the invention provides eukaryotic cells with modified cargo receptors as a tool for generating a variety of glycoproteins, the carbohydrate moiety of which is altered.

In the paragraph bridging pages 10 and 11 of the action, the Examiner asserts that the specification “does not provide sufficient structural and/or functional limitations” for the genus of “cargo receptor” or for the genus of “glycoprotein.” As it is well known in the art, however, “cargo receptor” means a type of receptor that is involved in transporting proteins, including glycoproteins, into a cell. By definition, “glycoprotein” connotes a group of conjugated proteins, each containing a carbohydrate as the non-protein component. As the foregoing paragraph explains, the present invention does not relate to a particular cargo

receptor or a particular glycoprotein, but to an inventive concept of modifying the carbohydrate moiety of a glycoprotein by alteration of a cargo receptor.

Rejections Under 35 U.S.C. §112 second paragraph

In Sections 16 and 17 of the Office Action, the Examiner has rejected claims 14-18 for indefiniteness. Applicants have amended Claim 14 to distinctly claim the subject matter of the invention. This revision is supported by the specification on page 9, in the second and third paragraphs, and on page 17, in the second paragraph.

On page 12, in the third paragraph of the action, the Examiner alleges that there is insufficient antecedent basis for the limitation “said cell” in Claim 14. Applicants respectfully disagree. The antecedent basis for “said cell” is a “*eukaryotic cell* comprising heterologous DNA coding for a cargo receptor that is characterized by an alteration of an amino acid in its carbohydrate recognition domain,” as recited in Claim 14 (emphasis added).

On pages 12, in the fourth and the fifth paragraphs, the Examiner has rejected Claim 17 for indefiniteness and insufficient antecedent basis for the limitation “said cells.” Applicants have amended Claim 17 to obviate the basis for the indefiniteness rejection. The antecedent basis for “said plurality” is a “plurality of eukaryotic cells,” as Claim 17 prescribes quite clearly.

As described throughout the specification, in particular, respective third paragraph on page 3 and page 4, heterologous DNA encoding a modified cargo receptor is introduced into a cell, then the cell expresses a glycoprotein which is processed by the modified cargo receptor, such that the glycoprotein has an altered carbohydrate moiety. Each cell may have heterologous DNA encoding a different cargo receptor. Therefore the resultant plurality of cells comprising a variety of modified cargo receptors may express glycoproteins with different carbohydrate moieties.

On page 13, in the first paragraph of the action, the Examiner has rejected Claim 18 for indefiniteness for the usage of term “particular.” Applicants submit that the specification amply defines a specific glycoform based on screening. For example, see pages 17 and 19.

As the specification describes, following random mutagenesis, the altered carbohydrate recognition domain of a cargo receptor is correlated with a certain type of glycoform, and then the specific alteration is carried out to obtain the corresponding glycoform. Accordingly, the rejection to Claim 18 should be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

In Sections 18-20 of the action, the Examiner has rejected Claims 14-18 for anticipation by Ueno *et al.* and Hirai *et al.*, respectively.

The publications teach production of a chimeric protein using ERGIC-53 (Ueno *et al.*) or VIP36 (Hirai *et al.*), along with MAH or BPA lectin and a glycoprotein. As a result, the lectin domain of ERGIC-53 or VIP36 is *entirely replaced* by MAH or BPA lectin, respectively. By contrast, the cargo receptor recited in Claim 14, is altered by at least one amino acid mutation in its carbohydrate recognition domain.

Although the lectin domains of ERGIC-53 and VIP36 may be similar structurally to MAH and BPA lectin, the chimeric proteins disclosed by the publications cannot function as a cargo receptor. This is so because neither MAH nor BPA lectin can dissociate from the carbohydrate after binding to the latter. The chimeric proteins of the publications localize in the Golgi and do not have mobility in the cell. On the other hand, the modified cargo receptor in the claimed invention recognizes the carbohydrate moiety of different glycoproteins and affects protein glycosylation and transportation, by controlling its binding to and dissociation from the carbohydrate (see specification at pages 6 and 7, respective second paragraph).

It is apparent, therefore, that neither reference discloses or even suggests each and every aspect of Applicants' claimed invention. By the same token, there is no basis for rejecting Claim 14 and its dependents for anticipation by the publications. Accordingly, the rejections in question should be withdrawn.

Rejections Under 35 U.S.C. § 102(a)

In Sections 21 and 22 of the action, the Examiner has rejected Claims 14-18 for anticipation under 35 U.S.C. 102(a) by the Master's Thesis of Sato and the Master's Thesis of Shimauchi, respectively.

On the strength of the accompanying declarations by each of co-inventors Sato and Shimauchi, however, Applicants demonstrate that the teachings invoked by the examiner in this regard constitute not the work of "another," as Section 102(a) requires, but rather that of the inventive entity. Thus, Applicants have eliminated the cited theses as citable prior art, thereby obviating the rejections at issue.

Rejections Under 35 U.S.C. § 103(a)

In Sections 23 and 24 of the action, the Examiner has rejected claims 14 and 16-18 for obviousness over Itin *et al.*

Itin *et al.* teach ERGIC-53 mutants with their mannose binding activity **abolished**, see for example, page 487, right column, line 11 to page 488, left column, line 21. There is no description or suggestion that ERGIC-53 of the reference has modified carbohydrate binding activity and thereby produces a glycoprotein with different glycoform. By contrast, the present invention relates to alteration of an amino acid in the carbohydrate recognition domain of a cargo receptor to produce a glycoprotein with different glycoform in a eukaryotic cell, as Claim 14 recites. Therefore, the carbohydrate binding activity of the cargo receptor in the invention is maintained, not abolished.

Armed with the teachings of this reference, therefore, the skilled artisan would not have considered it obvious, within the meaning of Section 103, to come up with a eukaryotic cell, as recited in Claim 14, or a plurality of eukaryotic cells per Claim 17.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that all of the pending claims are now in condition for allowance. An early notice to this effect is earnestly solicited. If there are any questions regarding the application, the Examiner is invited to contact the undersigned at the number below.

Respectfully submitted,

Date 12 July 2006

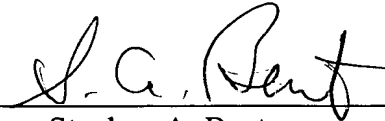
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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.